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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,200	04/18/2005	Roberto D'Alessio	17722 (PC27004)	5147

7590 01/18/2007

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EXAMINER	
FREISTEIN, ANDREW B	
ART UNIT	PAPER NUMBER
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,200	D'ALESSIO ET AL.	
	Examiner	Art Unit	
	Andrew B. Freistein	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-12,23-26 and 28-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-22 and 27* is/are rejected.

7)☐ Claim(s) *13-22 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20070104*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-32 are pending.

Priority

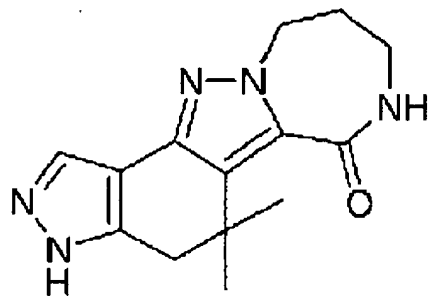
This application is a 371 of PCT/EP03/01594, filed 02/18/2003, which claims benefit of US Provisional Application No. 60/357,918, filed 02/19/2002.

Information Disclosure Statement

No information disclosure statement (IDS) was submitted.

Restriction Requirement

In a response filed 11/29/2006, Applicants elected (with traverse) the subject matter of Group VI, Claim 1-12 (in part) drawn to products of formula (I), containing compounds not encompassed in Groups I-V. Further, Applicants elected compounds of formula (Id) wherein B is pyrazole, r is 3 and A is CH_2-$C(CH_3)_2$ and the species:



In the restriction requirement, Group VI is drawn to claims 1-12. However, during a telephone conversation with Attorney Mark Cohen on 01/04/2007, Examiner and Attorney agreed that the elected group is claims 13-22 and 27 (in part), drawn to products of formula (Id).

Nevertheless, Examiner may reconsider to rejoin the method of use claims (claims 1-12) commensurate in scope with the product claims when and if the case is found to be in condition for allowance provided those method of use claims are free of 35 U.S.C. § 112 first and second paragraph issues (including written description, reach-through claim language and/or scope of enablement issues).

Applicants reserve their right to file one or divisional applications on the non-elected subject matter.

Applicants traverse the restriction requirement asserting that restriction is proper when an application has two or more independent and distinct inventions claimed and cites MPEP 802.01.

However, the instant application is a 371 of PCT/EP03/01594 and MPEP 803.01 is inapplicable. Rather, the instant application was restricted under a Lack of Unity of Invention practice. As described in the previous office action, PCT Rule 13.2 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention).

According to MPEP 1850,

> When the Markush grouping for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
>
> (A) All alternatives have a common property or activity; and
> (B) (1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
> (B) (2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.
>
> In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a

small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

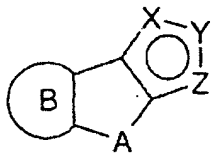
In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

The fact that the alternatives of a Markush grouping can be differently classified should not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention should be reconsidered by the examiner. Reconsideration does not necessarily imply that an objection of lack of unity shall be raised (emphasis added).

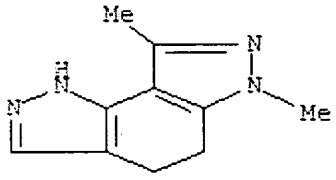
In the instant application, there is at least one Markush alternative that is not novel over the prior art.

Claim 13 of the instant application is drawn to a compound of formula (I)



, wherein X is CR_1; R_1 is lower alkyl; Y is N; Z is NR_1; A is $(CH_2)_m$; m is 2; and B is a 5-membered aromatic ring having 0 to 3 heteroatoms selected from S, O and N.

Le Tourneau et al., US Pat. No. 4,734,430 discloses the compound



(see col. 11, lines 63-67).

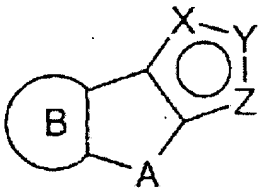
Because there is at least one Markush alternative that is not novel over the prior art and the Unity of Invention rules apply to the instant application, restriction was proper and is maintained.

Status of the Claims

Claims 13-22 & 27 (in part) are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR § 1.142(b). The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference that anticipates one invention would not render obvious the other invention.

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:

Compounds of the Formula (I), 

, wherein:

X is N or NR_1;

Y is N or NR_1;

Z is CR_1;

R_1 is as defined in claim 13;

B is 1*H*-pyrazole;

A is $(CH_2)_m$, $(CH_2)_n$-CH=CH-$(CH_2)_n$ or $(CR_zR_y)_p$;

R_z is as defined in claim 13;

R^y is as defined in claim 13;

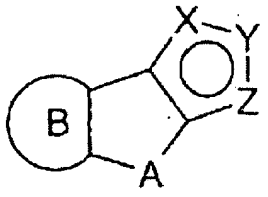
m is 2;

p is 2; and

n is 0.

Non-elected and Non-examined Subject Matter

The scope of the invention of the non-elected and non-examined subject matter is as follows:

Compounds of the Formula (I), 

, wherein:

X is S, O or CR_1;

Y is S, O or CR_1;

Z is N, NR_1, S or O;

B is a 5-membered aromatic ring other than 1*H*-pyrazole or a 6-memebered ring having 0 to 3 heteroatoms selected from S, O and N.

m is 1, 3 or 4;

p is 0, 1 or 3; and

n is 1 or 2.

As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 13-22 & 27 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as thiazolidine, piperazine, quinoline, thiophene, morpholine, oxazol, pyrimidine, pyrazine, pyran, etc. which are chemically recognized to differ in structure, function, and reactivity.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the elected/examined subject matter so that a reference which anticipates the elected/examined subject matter would not render obvious the non-elected subject matter.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-22 are 27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 13 and 17-19, the term "hydrido" is used as an alternative in variables R^1, R', R'', R_z, R_y, and R^2. A hydrido is a complex hydride containing a hydride ligand bonded to a central atom. The specification provides no explanation of what the complex hydride is and there is no example in the specification having a complex hydride. As a result, this term should be amended to "hydrogen."

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of the formula (I), isomers,

tautomers, carriers and pharmaceutically acceptable salts thereof, the specification does not reasonably provide enablement for prodrugs of compounds of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

1) the nature of the invention;
2) the state of the prior art
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the breadth of the claims;
7) the quantity of experimentation necessary; and ,
8) the level of skill in the art.

The Nature of the Invention

The nature of the invention is compounds of the formula (I), isomers, tautomers, carriers , prodrugs and pharmaceutically acceptable salts thereof.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that a prodrug is a pharmacological substance (drug) which is administered in an inactive (or significantly less active) form. Once administered, the prodrug is metabolised in the body in vivo into the active compound. A prodrug can be formed by various mechanisms and vary depending on the functional groups present in the parent compound. Moreover, different prodrugs arise from parent

compounds containing varying functional groups, such as a carboxylic acid, an alcohol, or an amine, all of which require different mechanisms.

The amount of direction or guidance presented and the presence or absence of working examples

The only direction or guidance present in the instant specification is for the compounds of formula I, pharmaceutically acceptable salts thereof and pharmaceutical compositions comprising compounds of formula I.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure. Specifically, the instant claims include any prodrug of a compound of formula I, without accurately describing how to prepare a prodrug.

The quantity of experimentation necessary

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare a prodrug of a compound of formula (I) as instantly claimed, because a prodrug can be formed by various mechanisms and vary depending on the functional groups present in the parent compound. The only guidance provided in the specification is for the compounds of formula (I) and pharmaceutically acceptable salts. There is no guidance or working examples present for prodrugs.

Therefore, the claims lack enablement and this rejection can be overcome by deleted the words "prodrugs" from the claims.

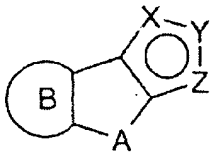
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-18 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Le Tourneau et al., US Pat. No. 4,734,430.

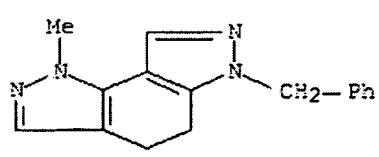
Claims 13-18 of the instant application is drawn to a compound of formula (I),



, wherein X is CR_1; R_1 is hydrido or lower alkyl; Y is N; Z is NR_1; A is $(CH_2)_m$ or $(CR_zR_y)_p$; m is 2; R_z is hydrido; R_y is hydrido; p is 2; B is a 5-membered aromatic ring having 0 to 3 heteroatoms selected from S, O and N; each of X, Y, Z and B rings are optionally further substituted with one or more L-R2 groups; L is a single bond or an alkylidene group; and R2 is hydrido, alkyl, or a 5-12 membered monocyclic ring having 0-3 heteroatoms.

Examiner interprets "hydrido" to be a hydrogen atom.

Le Tourneau et al., US Pat. No. 4,734,430 discloses the compounds



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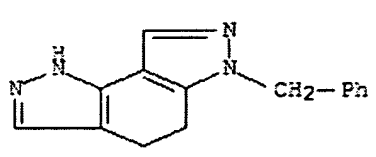

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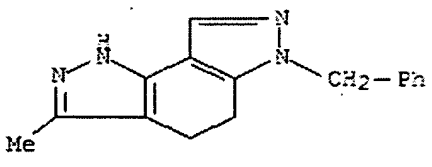

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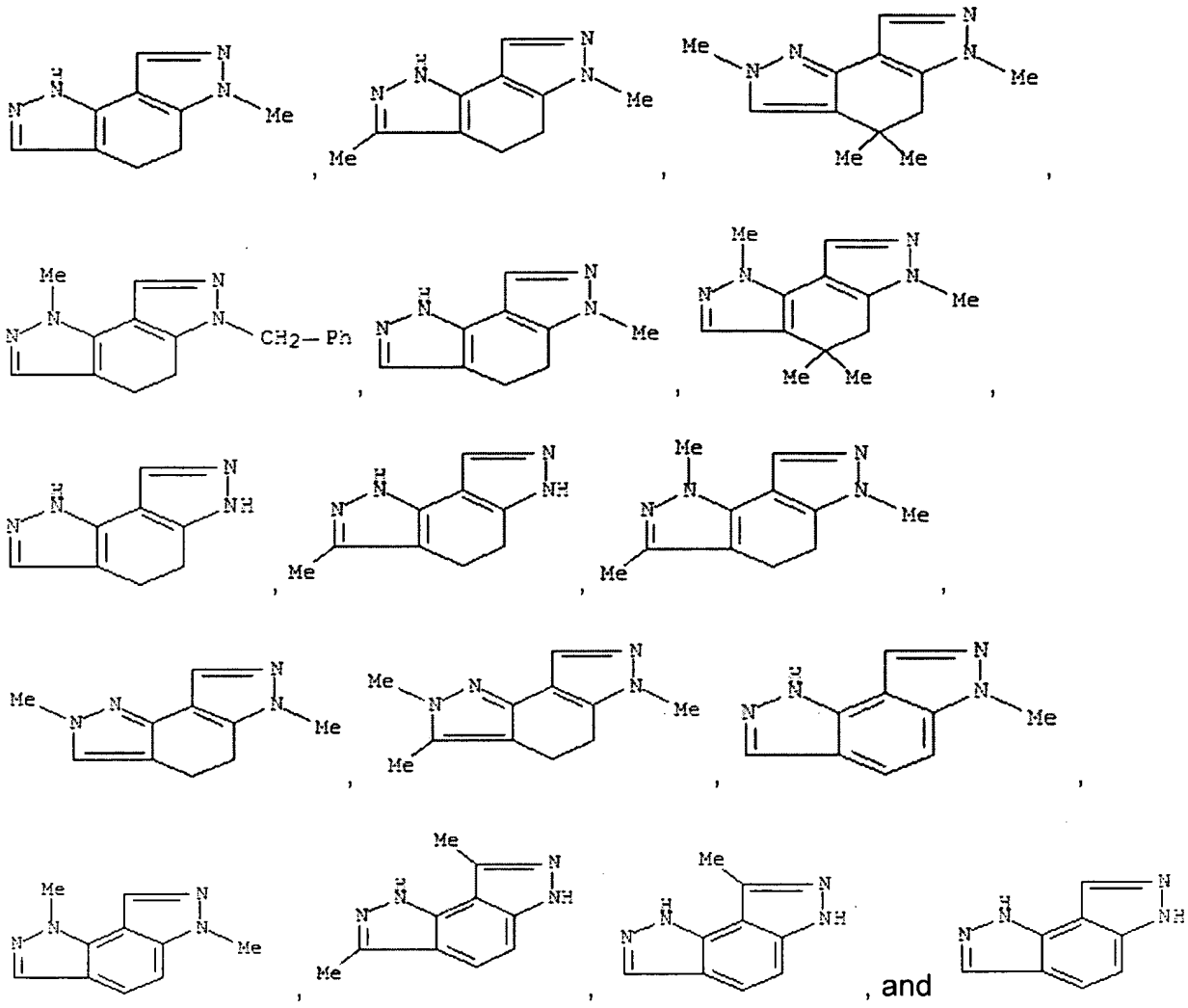

(see Le Tourneau, STN International, HCAPLUS Database, Columbus, OH, Accession No. 1988:454772, Reg. Nos. 115309-93-8, 115309-94-9, 115309-95-0, 115309-98-3, 115309-97-2, 115309-92-7, 115310-00-4, 115310-01-5, 115310-05-9, 115310-12-8, 115310-06-0, 115310-07-1, 115310-09-3, 115310-10-6 and 115310-11-7 (2007)).

Additionally, Le Tourneau et al. disclose pharmaceutically acceptable acid addition salts of the compounds and pharmaceutical compositions comprising the compounds (see US 4,737,430, col. 1, lines 40-61 and col. 5. lines 9-58).

Claim Objections

Claims 13-22 are objected to as being drawn to non-elected subject matter.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

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Patent Examiner, AU 1626

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Supervisory Patent Examiner, AU 1626
Date: January 5, 2007